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10/527,455	10/24/2005	Kozo Takeda	TAKEDA=19	2196

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,455	TAKEDA ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,8,9,11-17,19-22 and 24* is/are pending in the application.

4a) Of the above claim(s) *8,11-16,21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,9,17,19,20 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0211*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Request for Continued Examination of June 29, 2010, in response to the action mailed January 31, 2009, is acknowledged. It is acknowledged that Claims 10 and 23 have been cancelled, Claims 1, 4, 5, 9, and 19 have been amended, and Claim 24 has been added. Claims 1, 4, 5, 8, 9, 11-17, 19-22, and 24 are pending. The elected invention is directed to a method for removing DNA contaminants from a sample comprising an active protein, wherein the method comprises forming DNA particles in a low conductivity and low pH solution (Applicants' response of August 29, 2007). Claims 8, 11-16, 21, and 22 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b). Claims 1, 4, 5, 9, 17, 19, 20, and 24 are hereby considered.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112: The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 20, and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

For Claim 5, recitation of "according to claim 1, wherein the adjusted aqueous solution of step 1) is selected from aqueous solutions of hydrochloric acid, citric acid and acetic acid" renders the claim indefinite. Since Claim 1 encompasses adjusted aqueous solutions having a pH above pH 7, it is unclear how said solutions can be solutions of hydrochloric acid, citric acid, or acetic acid. The skilled artisan would not understand the metes and bounds of the recited invention.

Claim 20 is rendered indefinite for reciting dependence from a cancelled claim, Claim 23.

For Claim 24, the term "10o mM" renders the claim indefinite. It is unclear whether said term means "10 mM" or "100 mM". The skilled artisan would not understand the metes and bounds of the recited invention. For purposes of examination, it is assumed that "10o mM" means "100 mM".

Any subsequent rejection, based on clarification of the above phrases and terms, will not be considered a new ground for rejection.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Rejection of Claims 1, 4, 5, 9, 17, 19, 20, and 24 under 35 U.S.C. 112, first paragraph/written description, for reasons explained in the prior action, is maintained. In summary, the specification does not describe removal of DNA contaminants directly from cell culture lysates, culture medium, tissue homogenates and other complex protein-comprising samples such that the skilled artisan would recognize full possession. The specification only describes removal of DNA from a sample comprising an affinity purified antibody. Applicants did not provide any arguments regarding this basis of the rejection.

Claims 1, 4, 5, 9, 17, 19, 20, and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in

the relevant art that the Inventors, at the time the application was filed, had possession of the claimed invention. Claim 1 introduces the limitation of "wherein the protein is an antibody or a modified antibody which has an isoelectric point of above pH 4.0" The specification fails to describe said limitation and, thus, Claim 1, and dependent Claims 4, 5, 9, 17, 19, 20, and 24, are rejected under 35 U.S.C. 112, first paragraph, for introducing New Matter.

For these reasons and those explained in the prior action, Claims 1, 4, 5, 9, 17, 19, 20, and 24 are rejected under 35 U.S.C. 112, first paragraph/written description.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of Claims 1, 4, 5, and 10 under 35 U.S.C. 103(a) as being unpatentable over Oxenburch et al, 1965 in view of Kipriyanov et al, 1999, for reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments. These arguments are not found to be persuasive for the reasons following each argument.

(A) One of the important features of the presently claimed method is to form particles containing DNA contaminants by adjusting the pH and ionic concentration at the same time. To clarify this feature, the phrase "so as to form particles containing DNA contaminants" has been added to claim 1.

(A) Reply: It is acknowledged that Claim 1 has been amended to recite "so as to form particles containing DNA contaminants". However, this argument is not persuasive because (i) Claim 1 does not recite simultaneous adjustment of the pH and ionic strength and (ii) the specification does not teach simultaneous adjustment of the pH and ionic strength. Thus, the skilled artisan would understand Claim 1 to mean that, prior to step 2, the pH can be adjusted before or after adjustment of the ionic strength.

(B) Oxenburgh discloses methods of precipitating nucleic acids from a protein extract using streptomycin.

(B) Reply: See the Action of December 29, 2010, Reply (B).

(C) Oxenburgh neither teaches nor suggests adjusting the pH and ionic concentration for a sample solution. Moreover, there is nothing in Oxenburgh that teaches or suggests that such an adjustment relates to formation of particles containing DNA contaminants.

(C) Reply: See the Action of December 29, 2010, Reply (C).

Rejection of Claims 9, 19, and 20 under 35 U.S.C. 103(a) as being unpatentable over the combination of Oxenburch et al, 1965 and Kipriyanov et al, 1999 in view of Harlow et al, 1988, as evidenced by Fahrner et al, 1999, for reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments. There is absolutely nothing in any of the cited references that even suggests considering the isoelectric point of the solution when precipitating DNA contaminants. It is critical to the herein claimed method that both the pH and the ionic concentration be adjusted in order to precipitate DNA contaminates from a solution. This is neither shown nor suggested by any of the cited references, either alone or in combination. This is the same argument provided

by Applicants in their prior response. The argument is not found to be persuasive for the reasons explained in the Action of December 29, 2010, p11¶ 2.

Rejection of Claims 1, 4, 5, 9, 10, 18, and 19 under 35 U.S.C. 103(a) as being unpatentable over Lydersen et al, 1994 in view of Harlow et al, 1988, as evidenced by Fahrner et al, 1999, as explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants argue the following. The reasons these arguments are not persuasive are stated in each reply.

(A) The method disclosed in Harlow is for purifying an antibody by binding an antibody in a protein A column and washing and eluting the column. On the other hand, the method disclosed in Lydersen does not relate to the use of a protein A column. Thus, is it respectfully submitted that one skilled in the art could not possibly apply the method of Lydersen to that of Harlow, since the separation feature of Harlow is entirely different from that of Lydersen.

(A) Reply: As explained in the Action of March 9, 2009 (p14):

> "It would have been obvious to a person of ordinary skill in the art to combine the methods of Lydersen et al and Harlow et al. In said combined method, the antibody-containing, low salt solution obtained via the method of Harlow et al would be adjusted to a low pH in order to precipitate any contaminating DNA. Motivation to do so derives from the desire to remove the DNA contaminants in protein A-sepharose isolated antibodies (see Fahrner et al; Table I). Removal of said DNA contaminants is advantageous in the preparation of antibodies for treatment. The expectation of success is high, as all methods were known in the art."

(B) None of the cited references teaches or suggests that there is any relationship between pH and ionic concentration of a solution and DNA contaminant particle formation.

(B) Reply: The relationship between pH and ionic concentration of a solution and DNA contaminant particle formation is inherent to the method rendered obvious by the combination of Lydersen et al, 1994, Harlow et al, 1988, and Fahrner et al, 1999.

Rejection of Claim 17 under 35 U.S.C. 103(a) as being unpatentable over the combination of Lydersen et al, 1994, Harlow et al, 1988, and Fahrner et al, 1999 in view of Somack et al, 1999, for reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants argue that none of these references suggests that DNA contaminants can be precipitated form a protein-containing solution by controlling pH and isoelectric point along with the ionic concentration. This is the same argument provided in the response of September 9, 2009; see the Office's reply in the Action of January 31, 2009, p12¶1.

Rejection of Claim 20 under 35 U.S.C. 103(a) as being unpatentable over the combination of Lydersen et al, 1994, Harlow et al, 1988, and Fahrner et al, 1999 in view of Sigma, Inc, as described in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments. (i) The fact that Sigma teaches an aqueous solution of 500 mM Tris at pH 3.5-5.0 adds nothing to the cited references. There is no suggestion for using the Sigma solution in any of the methods of the cited references. (ii) Moreover, there is no teaching or suggestion for controlling the pH/isoelectric point and ionic concentration of the solution to be treated. This is the same argument provided in the response of September 9, 2009; see the Office's reply in the Action of January 31, 2009, p12¶3.

Claim 17 is herein rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Oxenburch et al, 1965 and Kipriyanov et al, 1999 in view of Somack et al, 1999. The combination of Oxenburch et al and Kipriyanov et al is described above and in the prior actions. Said combination does not teach use of filtration to remove the DNA precipitate. Somack et al teaches what was well-known in the art; that a DNA precipitate can be removed by

filtration through a filter (Example 1B). It would have been obvious to a person of ordinary skill in the art to adapt the method taught by the combination of Oxenburch et al and Kipriyanov et al to incorporate the teachins of Somack et al, wherein the centrifugation step of Oxenburch et al is replaced with filtration of the DNA precipitate, because said techniques are functionally equivalent. Motivation to do so is provide by the desire to remove the DNA precipitate and the ease of filtration for large numbers of samples. The expectation of success is high, as all methods are well-known in the art. Therefore, Claims 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Oxenburch et al, 1965 and Kipriyanov et al, 1999 in view of Somack et al, 1999.

In support of their request that the prior, analogous rejection of Claim 17 under 35 U.S.C. 103(a) as being unpatentable over Oxenburch et al, 1965 in view of Somack et al, 1999 be withdrawn, Applicants provide the following arguments, which are relevant to the rejection above. These arguments are not found to be persuasive for the reasons following each argument.

(A) Even though Somack discloses that precipitated DNA can be removed by filtration, Oxenburgh does not disclose how to form this DNA precipitate. There is nothing in Oxenburgh that even suggests adjusting the pH and the isoelectric point of a solution in order to precipitate DNA.

(A) Reply: See Reply (C), above regarding the rejection of Claims 1, 4, 5, and 10 under 35 U.S.C. 103(a) as being unpatentable over Oxenburch et al, 1965 in view of Kipriyanov et al, 1999.

(B) Oxenburgh did not even contemplate solutions of recombinant proteins.

(B) Reply: It is Kipriyanov et al, 1999 that teaches solutions of recombinant proteins.

For these reasons and those set forth in the prior actions, the above rejections under 35 U.S.C. 103(a), are maintained.

Allowable Subject Matter

No claims are allowable.

This is a continued examination of the instant application. All claims are drawn to the same invention claimed in the earlier filings and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered prior to the filing of the RCE. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this continued examination. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages. It is also requested that the serial number of the application and date of amendment be referenced on every page of the response.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652